

Appl. No. 09/520,130  
Amendment dated March 16, 2006  
Reply to Final Office Action of July 19, 2005 and Notice of Appeal of December 16, 2005

### **REMARKS**

Claims 59-60 have been amended for clarity. No new matter is added by the amendments. Claims 47-63 are pending in the application. Entry of the Amendment and reconsideration of the claims in view of the following Remarks is requested.

### **Withdrawn Rejections**

Applicants acknowledge the withdrawal of the rejection of claims 47-63 under 35 U.S.C. 112, second paragraph.

Applicants acknowledge the withdrawal of the rejection of claims 59 and 61-63 under 35 U.S.C. 112, first paragraph.

### **Interview Summary**

Applicants thank Examiner Holleran for the interview conducted on January 25, 2006. We discussed support in the specification for claims 47-52 in order to obviate the 112 written description rejection.

### **Double Patenting**

Applicants acknowledge the provisional rejection of claims 47-63 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-51 of copending Application No. 09/863,693. Applicants acknowledge the provisional rejection of claims 47-63 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39-49 of copending Application No. 09/373,403. Applicants acknowledge the provisional rejection of claims 47-63 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of copending Application No. 10/143,437. Applicants request that this rejection be held in abeyance until notice of allowable subject matter.

### **35 U.S.C. § 112, first paragraph**

Claims 47-52 were rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. The Examiner contends that the disclosure does not

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adequately describe multispecific antibodies comprising more than one light chain, wherein the light chains have at least 98% sequence identity, and only differ outside of the CDR regions Applicants traverse this rejection.

Applicants note that there is a strong presumption that an adequate written description of the claimed invention exists (*See MPEP 2163.II.A.*) The fundamental factual inquiry in whether the claims are sufficiently described "is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed." *MPEP 2163 I.B.* To adequately describe the claims, the specification need not describe *ipsis verbis* what is recited in the claims; rather, the claim limitations may be supported in the specification through implicit or inherent disclosure rather than express disclosure. *MPEP 2163 I.B.* Even if the specification does not explicitly recite a claim limitation, sufficient written description exists for the limitation if one of skill in the art can "immediately discern the limitation" from reading the original specification. *Waldemar Link, GmbH & Co. v. Osteonics Corp.*, 31 USPQ2d 1855 (Fed Cir. 1994). "If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met." *MPEP 2163 II.A.3(a)*. In light of the foregoing standards, the present claims are clearly adequately described by the specification.

Claims 47-52 recite a bispecific antibody comprising a first polypeptide and a second polypeptide, and first and second light chain variable domains each having three CDR regions, wherein the first and second light chain variable domains have at least 98% sequence identity, and only differ from one another at amino acid positions outside of the CDRs. Applicants submit that one of skill in the art at the time of filing would have clearly understood from reading the specification that Applicants were in possession of the claimed bispecific antibodies at the time of filing.

The Applicants respectfully disagree, and submit that the specification does disclose the use of light chains having less than 100% identity, for example, having at least 98% identity. As stated in the previous Response, the Applicants explicitly disclose two light chains that have 98% sequence identity and differ by residues outside of the antigen binding CDRs. The specification states that these amino acid changes may have little or no effect on antigen binding

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(page 97, lines 26-27). The specification concludes that, while the sequence similarity of these light chains makes them candidates for the common light chain of the invention, in an alternative embodiment "according to the invention, such light chains having 98-99% sequence identity with the light chain of a prospective paired scFv (Ax1.78, for example), *may be substituted with the paired light chain and retain binding specificity*" (page 97, line 28 through page 98, line 3) (emphasis added). Applicants submit that one of skill in the art would understand that this embodiment is an alternative to using these light chains as the common light chain and that they each may be substituted for the paired light chain in a scFv specific for Ax1.83 and retain binding specificity for that antigen.

For example, if one of skill in the art reading the specification wanted to create a bispecific antibody comprising anti-Ax1.78 and anti-Rse specificity, they could do so by using the Ax1.78 light chain as a common light chain. Alternatively, the Ax1.78 light chain could be substituted with the Rse.04 light chain and paired with Ax1.78 heavy chain and the Rse.04 light chain could be substituted with Ax1.78 light chain and paired with the Rse.04 heavy chain. Since each light chain could also pair with its corresponding heavy chain, there is no mispairing of the light chains in the method as claimed. The statement at page 97, line 26, to page 98, line 4, with regard to amino acids changes making no difference in antigen specificity coupled with the indication that any of the light chains could be substituted for the paired light chains indicates the exemplified light chain variable domains of Figure 4 are interchangeable with one another and can pair with any of the heavy chains.

Moreover, Applicants further submit the specification contemplated using scFv having different specificities to prepare multispecific antibodies. See the specification at pages 24-25, wherein the specification indicates the first and second polypeptides can include antibody variable domain polypeptides. In addition, Example 4, describes the use of scFv library and variable domain sequences from the library to prepare a bispecific antibody. See page 97, line 29, to page 101, line 5.

Thus, Applicants submit one of skill in the art reading the specification would understand the specification to provide written description for claims 47-52.

Applicants respectfully submit that claims 47-52 are amply described in the specification, for at least the foregoing reasons. Withdrawal of the rejection is respectfully requested.

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### **Claim Objections**

Claims 59 and 60 were objected to for the phrase "variable light chain domain." In accordance with the Examiner's suggestion, these claims have been amended to recite a "light chain variable domain" for purposes of consistency. Withdrawal of this rejection is requested.

### **Interview**

The Applicants hereby request an interview with the Examiner and her supervisor to discuss any remaining rejections. The Examiner is requested to telephone the undersigned Applicants' representative to schedule the interview.

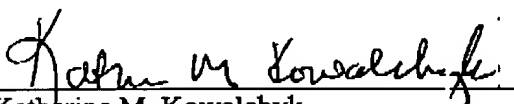
### **Summary**

Applicants submit that all pending claims are in condition for allowance, and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicants' representative if prosecution may be assisted thereby.

Respectfully submitted,

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